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ART 31

CLAIMS

5                   1. Nucleic acid molecule which corresponds to  
at least 70% of the SEQ ID NO. 1 or its complementary  
strand.

                  2. Nucleic acid molecule which corresponds to  
at least 90% of the SEQ ID NO. 1 or its complementary  
10 strand.

                  3. Isolated nucleic acid molecule comprising  
at least the SEQ ID NO. 1, its complementary strand or a  
portion thereof, having more than 15 nucleotides able to  
identify or reconstitute SEQ ID NO. 1 or its complementary  
15 strain.

                  4. Peptide encoded by the nucleic acid  
molecule according to any of the preceding claims.

                  5. Peptide according to the claim 4, having  
the following amino acid sequence of SEQ ID NO. 2 :  
20 Phe-Gly-Gly-Phe-Thr-Gly-Ala-Arg-Lys-Ser-Ala-Arg-Lys-Leu-  
Ala-Asn-Gln, or agonists of its receptor(s).

                  6. Peptide according to the claim 5,  
characterized in that it is a ligand of the ORL<sub>1</sub> receptor,  
preferably a mammal ORL<sub>1</sub> receptor, more specifically the  
25 human ORL<sub>1</sub> receptor.

                  7. Peptide according to the claim 4, having  
the following amino acid sequence of SEQ ID NO. 3 :  
Phe-Ser-Glu-Phe-Met-Arg-Gln-Tyr-Leu-Val-Leu-Ser-Met-Gln-  
Ser-Ser-Gln, or agonists of its receptor(s).

30                   8. Peptide according to the claim 4, having  
the following amino acid sequence of SEQ ID NO. 4 :

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Thr-Leu-His-Gln-Asn-Gly-Asn-Val, or agonists of its receptor(s).

9. Inhibitor directed against the nucleic acid molecule according to any of the claims 1 to 4, the peptide according to any of the claims 4 to 8 or the receptor(s) of said peptide.

10. Inhibitor according to the claim 9, characterized in that it is a polyclonal or monoclonal antibody or a portion thereof, directed against the peptide according to any of the claims 4 to 8 or its receptor.

11. Inhibitor according to the claim 9, which is an antisense oligonucleotide which has a sequence capable of specifically binding to the nucleic acid molecule according to any of the claims 1 to 3 so as to prevent its transcription and/or its translation.

12. Inhibitor according to the claim 11, comprising chemical analogs of nucleotides.

13. Inhibitor according to the claim 11, said oligonucleotides having sequences which differ from one another at predefined positions.

14. Inhibitor according to any of the claims 11 to 13, wherein the oligonucleotide is coupled to a substance which inactivates the nucleic acid according to any of the claims 1 to 3.

15. Inhibitor according to the claim 14, wherein said substance is a ribozyme.

16. Inhibitor according to the claim 9, characterized in that it is an antagonist to the receptor of the peptide according to any of the claims 4 to 8.

17. Vector comprising the nucleic acid molecule according to any of the claims 1 to 3.

18. Pharmaceutical composition comprising an element chosen among the group consisting of the nucleic acid molecule according to any of the claims 1 to 3, the peptide according to any of the claims 4 to 8, the inhibitor according to any of the claims 9 to 16 and/or the vector according to the claim 17, and a pharmaceutically acceptable carrier.

19. Pharmaceutical composition comprising an amount of a substance effective to reduce the expression and/or the "effects" resulting from expression of the peptide according to any of the claims 4 to 8, and a pharmaceutically acceptable carrier.

20. Pharmaceutical composition comprising an amount of a substance effective to reduce the expression and/or the "effects" resulting from expression of the nucleic acid molecule according to any of the claims 1 to 3.

21. Pharmaceutical composition according to any of the claims 18 to 20, for the treatment and/or the prevention of a disease related to the following functions and/or behaviours : hyperalgesia, neuroendocrine secretion, stress, locomotor activity, anxiety, instinctive behaviour, decreasing of learning, memory, curiosity, attention and/or sensory perception.

22. Transgenic non-human animal which comprises the nucleic acid molecule according to any of the claims 1 to 3.

23. Method for recovering an inhibitor not known to be capable of specifically binding to a peptide according to any of the claims 4 to 8 can specifically bind to it, which comprises contacting the peptide according to any of the claims 4 to 8 under conditions permitting

binding of a inhibitor known to bind the peptide according to any of the claims 4 to 8, determining the presence of any inhibitor bound to said peptide and recovering said inhibitor.

5                   24. Method for recovering a compound not known to be capable of specifically binding as an antagonist or as an agonist of the peptide according to the claim 6 to a  $ORL_1$  receptor, preferably a mammal  $ORL_1$  receptor, specifically a human  $ORL_1$  receptor, can  
10 specifically bind to said receptor, which comprises contacting a cell, preferably a mammalian cell, comprising a vector adapted for expression in a mammalian cell, which vector further comprises nucleic acid molecule which expresses said  $ORL_1$  receptor on the cell's surface, with  
15 the compound under conditions permitting binding of the peptide known to bind to said receptor, detecting the presence of any compound bound to said receptor, and recovering said compound.

20                   25. Method for recovering a compound not known to be capable of specifically binding as an antagonist or as an agonist of the peptide according to the claim 6 to an  $ORL_1$  receptor, preferably a mammal  $ORL_1$  receptor, specifically a human  $ORL_1$  receptor, can  
25 specifically bind to said receptor, which comprises preparing a cell extract from cells, preferably of mammalian cells, which comprises a vector adapted for expression in said cells, which vector further comprises nucleic acid molecule which expresses said receptor on the cell's surface, isolating a membrane fraction from the  
30 cells extract, incubating the compound with the membrane fraction under conditions permitting the binding of the peptide known to bind to said receptor, detecting the

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presence of any bound compound, and recovering said compound.

26. Method for recovering a compound which is not known to be capable of binding as an antagonist or as an agonist of the peptide according to the claim 6 to an ORL<sub>1</sub> receptor, preferably a mammal ORL<sub>1</sub> receptor, more specifically a human ORL<sub>1</sub> receptor, and prevent the peptide according to the claim 6, to activate said receptor, which comprises contacting a cell, preferably a mammalian cell, which cell comprising a vector adapted for expression in said cell, such vector further comprising nucleic acid molecule which expresses said receptor on the cell's surface with the compound under conditions permitting measure of a functional response, determining whether the compound prevents the peptide to activate said receptor, and recovering said compound.

27. Method according to the claim 24, wherein the cell is a non-neuronal cell, comprising the cellular components necessary to produce a second messenger and wherein the determination (of whether the compound blocks the activation of the ORL<sub>1</sub> receptor by a peptide according to the claim 6 or mimics inactivation of the ORL<sub>1</sub> receptor by a peptide according to the claim 6) comprises detecting the change in the concentration of the second messenger.

28. Method according to the claim 27, wherein the second messenger is chosen among the group consisting of cyclic AMP (cAMP), inositol phosphate metabolite or intracellular calcium.

29. Method according to the claim 28, wherein the modification of the second messenger is monitored by a secondary production of a report molecule chosen among the group consisting of luciferase, -galactosidase,

chloramphenicol acetyltransferase or growth hormone, or by the physiological modification of the cell, preferably monitored by measure of the extra-cellular pH.

30. Method according to any of the claims 27 to 29, wherein the non-neuronal cell is CHO.

31. Compound identified by the method according to any of the claims 23 to 30.

32. Pharmaceutical composition comprising the compound according to the claim 31 and a pharmaceutically acceptable carrier.

33. Diagnostic and/or dosage device comprising an inhibitor according to any of the claims 9 to 16, the peptide according to any of the claims 4 to 8 and possibly its receptor(s), preferably the ORL<sub>1</sub> receptor.

34. Method of genetic treatment or prevention of a disease induced by the nucleic acid sequence or the peptide according to any of the claims 1 to 8 in an animal, specifically in a human, wherein an inhibitor according to any of the claims 9 to 16 or a nucleic acid molecule encoding said inhibitor is administered to a patient with a pharmaceutically acceptable carrier to reduce the expression and/or the "effects" resulting from expression of said nucleic acid sequence or said peptide.

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